IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.:	10/758,415
Applicant:	William S. Brusilow
Filed:	January 16, 2004
TC/A.U.:	1614
Examiner:	Zohreh Vakili
Docket No. :	2930-109
Customer No.:	06449
Confirmation No. :	5654

Response

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

November 10, 2009

Sir:

In response to the Office Action of June 11, 2009, applicants have the following comments.

Claims 1-5, 10-11 and 21 were rejected under 35 USC §103(a) as unpatentable over Apostolakis or Ginefri-Gayet in view of Liedtke, further in view of Feurerstein. As pointed out in previous responses, Apostolakis discloses that MSO is a centrally acting neurotoxin with convulsive properties. Apostolakis also teaches that MSO can cause deformation, atrophy, loss of striation of muscle fibers, fibrosis and degeneration of Purkinje cells in the cerebellum. Apostolakis concludes that administration of MSO to rabbits in addition to the known convulsive effects may also be responsible for hind leg myopathy. The MSO dosage used by Apostolakis was 3-8 mg/kg body weight. Apostolakis does not suggest or disclose that MSO can be used to treat polyglutamine diseases such as Huntington's disease, spinocerebellar ataxia, and spinobulbar muscular atrophy and in view of the undesirable side effects discussed in Apostolakis

(i.e. convulsions, deformation, atrophy, loss of striation of muscle fibers, fibrosis and degeneration of Purkinje cells in the cerebellum) one skilled in the art would not be motivated to administer MSO to patients with a polyglutamine disease.

Ginefri-Gayet does not cure the deficiencies in Apostolakis as Ginefri-Gayet discloses that MSO, when administered at a convulsant dose (100-200 mg/kg body weight administered intraperitonealy or 50-75 µg per rat administered by ICV injection) induces a decrease in body temperature. Ginefri-Gayet indicates that MSO elicited a time dependent regional perturbation of 5-HT metabolism which could be due to the marked rise in ammonia levels caused by the irreversible inhibition of the activity of glutamine synthetase. Ginefri-Gayet suggests that the 5-HT receptor plays a role in MSO elicited hypothermia in the rat. Ginefri-Gayet does not suggest or disclose that MSO can be used to treat polyglutamine diseases such as Huntington's disease, spinocerebellar ataxia, or spinobulbar muscular atrophy and in view of the undesirable side effect (hypothermia), one skilled in the art would not be motivated to treat patients with polyglutamine diseases with MSO in view of the disclosure in Apostalakis and Ginefri-Gayet.

Applicants are unclear as to how Liedtke is related to the presently claimed invention as Liedtke is directed to an ion channel VR-OAC. The only mention of MSO in Liedtke is in paragraph 207 which discusses mammalian expression vectors such as a glutamine synthetase/ methionine sulfoximine co-amplification vector such as pEE14. There is no suggestion or disclosure regarding the administration of MSO for treating a polyglutamine disease. The office action states on page 4 that Liedtke teaches a glutamine synthetase/methionine sulfoximine co-amplification vector which reads on

claims 10 and 11. Applicants are unclear as to how this is related to the present claims as mammalian expression vectors are not part of the present invention nor are they mentioned in claims 10 and 11. In any case. Liedtke does not cure the deficiencies in Apostalakis and Ginefri-Gayet as Liedtke does not suggest or disclose that MSO can be used to treat polyglutamine diseases such as Huntington's disease, spinocerebellar ataxia, or spinobulbar muscular atrophy or suggest that the undesirable side effects disclosed in Apostalakis and Ginefri-Gayet can be avoided.

Feurerstein is directed to a method for treating a polyglutamine disorder using 2-pyrrolidinone derivatives. Feurerstein does not teach the use of MSO and thus does not cure the deficiencies in Apostalakis, Ginefri-Gayet and Liedtke as discussed above. If one skilled in the art combined the disclosures of Apostalakis, Ginefri-Gayet, Liedtke and Feurerstein, they would conclude that the administration of MSO leads to undesirable side effects such as deformation, atrophy, loss of striation of muscle fibers, fibrosis, degeneration of Purkinje cells in the cerebellum, decrease in body temperature, and regional perturbation of 5-HT metabolism which could be due to the marked rise in ammonia levels caused by the irreversible inhibition of the activity of glutamine synthetase, as MSO is a centrally acting neurotoxin with convulsive properties. None of the cited references alone or in combination suggest that MSO can be used to treat polyglutamine diseases such as Huntington's disease, spinocerebellar ataxia, or spinobulbar muscular atrophy and in view of the side effects disclosed in the prior art, one skilled in the art would not be motivated to test MSO for the treatment of such diseases. In view of the above discussion, applicants request that this rejection be withdrawn.

Applicants respectfully submit that all of claims 1-5, 10-11 and 21 are now in condition for allowance. If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

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